

REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the reasons that follow.

I. Status of the claims

The Advisory Action states that the claim amendments filed December 22, 2009, are not entered. Accordingly, the foregoing amendments are made to the claims pending before the Office as of the Office Action of July 21, 2008.

Claims 1-3 and 5 are cancelled and claims 4, 6 and 21 are amended. The subject matter of previously pending claims 2-4 is combined into new claim 4, which is now independent. The amendment to claim 6 reflects the amendment made to claim 4, from which it depends. Claim 21 is amended to depend from claim 4, which amendment is supported by the specification at, for example, page 8, lines 4-6, and Example 11, on page 31, lines 12 to 15. No new matter is added.

The foregoing amendments are made solely to advance prosecution and not in acquiescence to any rejection. The amendments are also made without prejudice or disclaimer of any subject matter removed by amendment or cancellation and reserving the right to pursue such subject matter in continuing applications.

Claims 7-20 are withdrawn as directed to methods and processes. Upon the identification of allowable subject matter in the pending composition claims 4, 6 and 21, Applicants request rejoinder and examination of claims 7-20.

Claims 4 and 6-21 are pending, with claims 4, 6 and 21 under examination.

II. Rejection of claim 4 under the written description provision of 35 U.S.C. § 112, first paragraph

The rejection of claim 4 was maintained for an alleged failure of the specification to provide sufficient written description for “HBV-like particles [containing] precore protein of claim 1, further not comprising HBV DNA therein.” Advisory Action at page 2. At the same time, the Advisory Action states that “HBcrAg (1) and HBcAg (2) are capable of

forming core-like particles without DNA, but they are not HBV-like particles.” Solely to advance prosecution, Applicants have amended claim 4 to conform its scope to that which the Examiner considers supported by the specification. It is respectfully believed that the rejection is overcome.

III. Rejection of claims 1 and 3-6 under the enablement provision of 35 U.S.C. § 112, first paragraph

Applicants respectfully traverse the rejection of claims 1 and 3-6 but, solely to advance prosecution, have cancelled claims 1, 3 and 5, and amended claims 4 and 6. As a result, the rejection of claims 1, 3 and 5 is rendered moot. To the extent that the rejection applied to claims 4 and 6 for recitation of “HBV virus-like particle” this, too, is rendered moot by amendments to claims 4 and 6 to remove that basis of rejection. Accordingly, the sole remaining issue is whether the specification enables the person of ordinary skill to make and use an isolated HBV core-like particle comprising an isolated HBV precore protein wherein the N-terminus of the precore protein is at position –28 and the C-terminus is at a position from 150 to 154, as set forth in SEQ ID NO: 1, further not comprising HBV DNA therein.

Examples 1 and 2 of the specification demonstrate isolation of HBV core-like particles not containing HBV DNA using sucrose density gradient centrifugation and gel filtration with Nonidet P-40. *See* Figure 4. Thus, the claimed invention is enabled and it is respectfully believed that the rejection is overcome.

IV. Rejection of claim 21 under 35 U.S.C. § 102(b)

The rejection of claim 21 was maintained as allegedly anticipated by Takahashi *et al.* *J. Immunol.* 147:3156-3160 (1990) (“Takahashi”) in part because the December 22, 2008, amendment to claim 21 was not entered. Advisory Action at page 2. Applicants respectfully traverse. In view of the foregoing amendment to claim 21, it is respectfully believed that the rejection is overcome. Takahashi does not disclose an assay kit and a diagnostic reagent for determining an antibody against the isolated HBV core-like particle having an antigenicity different from HBc antigen and HBe antigen, comprising an isolated HBV core-like particle comprising an isolated HBV precore protein, wherein the N-terminus of the precore protein is

at position -28 and the C-terminus is at a position from 150 to 154, as set forth in SEQ ID NO: 1, further not comprising HBV DNA therein.

Please reconsider and withdraw the rejection.

V. Rejections under 35 U.S.C. § 103

The Office maintained the rejection of claims 1-4 as allegedly obvious over Takahashi and Kobayashi *et al.*, *Gene* 30:227-232 (1984) (“Kobayashi”). *See* Advisory Action at pages 2-3. Claims 1-3 are cancelled, and Applicants respectfully traverse the rejection as it may have been applied to pending claim 4.

The Office cites to *Ex parte Anderson* 30 U.S.P.Q.2d 1866 for the contention that a single amino acid change is an obvious variant of the prior art. However, that decision was based not only on the obviousness of an allelic variant, but that Anderson had not provided rebuttal evidence concerning the properties of the resulting protein:

What is of concern in the consideration of rebuttal evidence are the properties of the DNA itself and/or the product it produces, *i.e.*, the protein it codes for. Appellants have not provided evidence that the protein coded for by the claimed DNA is any different from that of the prior art in its chemical properties.

Anderson 30 U.S.P.Q.2d at 1869. In the present situation, nonobviousness does not rely solely on a single amino acid difference.

Kobayashi teaches the DNA sequence and a predicted protein sequence, but is silent regarding particle-forming properties. Takahashi describes HBV precore products comprising p21c, p20, p18 and p17 of which only one p21c can form a particle. The p21c protein (a) lacks the signal sequence of amino acids -29 to 1, and (b) extends to amino acid 183. The invention of claim 4 differs from Takahashi that it forms HBV core-like particles with HBV precore protein, wherein the N-terminus of the amino acid sequence is at amino acid -28 and the C-terminus is at amino acid 150 to 154. These structural characteristics are completely different from those of the p21c protein. Accordingly, the combination of Kobayashi and Takahashi fails to provide all elements, and so cannot sustain a *prima facie* case of obviousness.

Moreover, according to Example 11, on page 31, lines 12 to 15, the particulate HBV precore protein of the present invention possesses antigenicity different from those of HBc antigen and HBe antigen. Therefore, the HBV core-like particle of claim 4 is further nonobvious over the cited art.

Further, Takahashi *teaches away* from the present claims. Only p21c, having the full length C-terminus, can form particles, whereas p20e, p18e and p17e, which lack the full C-terminus, cannot form particles. This disclosure of Takahashi suggests that the full length C-terminal sequence is necessary to form particles, and so a protein possessing amino acids –28 to 150-154 would not be expected to form particles. The presently claimed particles are, therefore, surprising in view of the teaching away by Takahashi.

For all of these reasons, Applicants respectfully believe that the pending rejection is overcome and should be withdrawn.

VI. Request for interview

If the Examiner does not consider allowable the claims presently under examination, Applicants respectfully request an interview. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance prosecution.

CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Commissioner is hereby authorized to charge any additional fees, which may be required under 37 C.F.R. §§ 1.16-1.17, and to credit any overpayment to Deposit Account No. 19-0741. Should no proper payment accompany this paper, then the Commissioner is authorized to charge the unpaid amount to the same deposit account. If any extension is needed for timely acceptance of submitted papers, then Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorize payment of the relevant fee(s) from the deposit account.

Respectfully submitted,

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